



PHARMACY COVERAGE GUIDELINES
SECTION: MEDICATIONS

NEXT REVIEW DATE: 4th QTR 2012

ORIGINAL EFFECTIVE DATE: 12-2-2011
LAST REVIEW DATE: 4-5-12
LAST CRITERIA REVISION DATE: NA
ARCHIVE DATE: NA

FENTANYL: ORAL, SUBLINGUAL, AND NASAL FORMULATIONS

Abstral™ (FENTANYL SUBLINGUAL TABLET)
Actiq™ (FENTANYL TRANSMUCOSAL LOZENGE)
Fentora™ (FENTANYL BUCCAL TABLET)
Lazanda™ (FENTANYL NASAL SPRAY)
Onsolis™ (FENTANYL BUCCAL SOLUBLE FILM)
Subsys™ (FENTANYL SUBLINGUAL SPRAY)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety. The guideline is not a guarantee of coverage.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available. The guideline in effect on the date of service will determine coverage.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

Description:

Oral and nasal formulations of the opioid analgesic fentanyl citrate are indicated only for the management of breakthrough cancer pain in individuals, who are already receiving opioid pain medication around-the-clock for cancer pain and who are tolerant to opioid therapy for their persistent cancer pain.

Substantial differences exist in the pharmacokinetic profiles of each product formulation that result in clinically important differences in extent of absorption of fentanyl. The formulations are not interchangeable on a mcg for mcg basis. There are no dose conversion directions available on any other fentanyl product; this includes oral, transdermal, or parenteral formulations.

Abstral sublingual tablet contains fentanyl citrate intended for oral sublingual administration. It is designed to be placed under the tongue and allowed to completely dissolve. It is available as 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, and 800 mcg strengths.



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Actiq transmucosal lozenge contains fentanyl citrate formulated as a solid drug matrix on a handle intended for oral transmucosal administration and is designed to dissolve slowly in the mouth. It is available as 200 mcg, 400 mcg, 600mcg, 800 mcg, 1200 mcg, and 1600 mcg strengths.

Fentora buccal tablet contains the opioid fentanyl citrate intended for buccal mucosal administration. It is designed to be placed and retained within the buccal cavity for a sufficient period of time to allow disintegration of the tablet and absorption of fentanyl across the oral mucosa. It is available as 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, and 800 mcg strengths.

Lazanda nasal spray is a liquid formulation of fentanyl citrate intended for intranasal transmucosal administration. It is formulated to deliver a spray of 100 mcL of solution containing 100 mcg or 400 mcg of fentanyl base, depending on product strength. It is supplied in a 5.3 mL bottle containing 8 meter dosed sprays.

Onsolis buccal soluble film delivers the opioid fentanyl citrate through the mouth's mucous membranes. Onsolis delivers fentanyl via an absorbable film that sticks to the inside of the cheek. It is available as 200 mcg, 400 mcg, 600 mcg, 800 mcg, and 1200 mcg strengths.

Subsys sublingual spray contains fentanyl base and is intended for sublingual administration. It is formulated in blister packages that contain single spray units of fentanyl base. It is available in 100 mcg, 200 mcg, 400 mcg, 600 mcg, and 800 mcg dosage strengths.



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FENTANYL: ORAL, SUBLINGUAL, AND NASAL FORMULATIONS (cont.)

Precertification:

Precertification* is required for Fentanyl oral, sublingual, or nasal formulations for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) retail prescription benefit. Medications requiring precertification are identified on the following list located on the Internet at <http://www.azblue.com/pdfs/medications/pharmacy/QLList.pdf>:

"Prescription Limitations and Precertification Requirements for Retail and Mail Order Prescriptions"

This list may also be requested by calling (602) 864-4273 or (800) 232-2345, ext. 4273.

Please refer to this list for Fentanyl oral, sublingual, or nasal formulation maximum dosage and other drug limitations.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Criteria:

➤ **Under the member's BCBSAZ retail prescription benefit**, Abstral or Fentora or Lazanda or Onsolis or Subsys are considered **medically necessary** for individuals 18 years of age* and older with documentation of **ALL** of the following:

1. Individual has cancer
2. Individual has breakthrough cancer pain
3. Individual is already receiving around-the-clock opioid therapy for underlying persistent cancer pain **and** is tolerant to the around-the-clock opioid therapy. Tolerance is determined by documentation of **ONE** of the following:
 - Individual is taking at least 60 mg of oral morphine daily
 - Individual is using at least 25 mcg of transdermal fentanyl/hour
 - Individual is taking at least 30 mg of oral oxycodone daily
 - Individual is taking at least 8 mg of oral hydromorphone daily
 - Individual is taking at least 25 mg of oral oxymorphone daily
 - Individual is taking an equianalgesic dose of another opioid for a week or longer

* Safety and efficacy has not been established in pediatric patients below the age of 18 years.

➤ **Under the member's BCBSAZ retail prescription benefit**, Actiq is considered **medically necessary** for individuals 16 years of age† and older with documentation of **ALL** of the following:



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1. Individual has cancer
 2. Individual has breakthrough cancer pain
 3. Individual is already receiving opioid therapy for underlying persistent cancer pain **and** is tolerant to the opioid therapy. Tolerance is determined by documentation of **ONE** of the following:
 - Individual is taking at least 60 mg of oral morphine daily
 - Individual is using at least 25 mcg of transdermal fentanyl/hour
 - Individual is taking at least 30 mg of oral oxycodone daily
 - Individual is taking at least 8 mg of oral hydromorphone daily
 - Individual is taking at least 25 mg of oral oxymorphone daily
 - Individual is taking an equianalgesic dose of another opioid for a week or longer

† Safety and efficacy of Actiq has not been established in pediatric patients below the age of 16 years.



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FENTANYL: ORAL, SUBLINGUAL, AND NASAL FORMULATIONS (cont.)

Criteria: (cont.)

- Fentanyl oral, sublingual, and nasal formulations for all other indications not previously listed is considered ***experimental or investigational*** based upon:
 1. Lack of final approval from the Food and Drug Administration, and
 2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
 3. Insufficient evidence to support improvement of the net health outcome, and
 4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
 5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Non-opioid tolerant individuals
- Management of acute pain
- Management of postoperative pain
- Management of headaches
- Management of migraine headaches
- Dental pain
- Use in the emergency department
- Management of chronic pain caused by a condition or diagnosis other than cancer

<u>History:</u>	<u>Date:</u>	<u>Activity:</u>
Director Pharmacy Mgmt review	02/06/12	Added Subsys information to Description, Criteria, and Resources section. Added to Resources a statement regarding review of package insert for complete dosing information
Director Pharmacy Mgmt review	10/24/11	Consolidation of Abstral, Actiq, Fentora, and Onsolis coverage guidelines into a single document. Addition of Lazanda to coverage guideline. Restatement and streamlining dosing information on each product in the Resource section. Deletion of unneeded information on dosing information on each product in the Resource section.
Director Pharmacy Mgmt review	09/16/11	Annual review, minor revisions, legal disclaimer added
Medical Policy Dept review	10/12/10	Updated disclaimer; removed Note section
Director Pharmacy Mgmt review	03/25/10	Adopted guideline (effective 04/08/10)
Medical Policy Panel review	03/09/10	Development
Director Pharmacy Mgmt review	03/03/10	Development



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Criteria Revisions:



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Resources:

Refer to package inserts for complete information on initial dosing, dose titration, and maintenance dosing.

Brief overview on dosing:

FDA Product Approval Information for ABSTRAL:

- FDA-approved indication:
ABSTRAL is an opioid analgesic indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are already taking around-the-clock opioid medicine.
- FDA-approved dosing information:
 - Initial dose of ABSTRAL: 100 mcg
 - Individually titrate to a tolerable dose that provides adequate analgesia
 - No more than two doses can be taken per breakthrough pain episode
 - Wait at least 2 hours before treating another episode of breakthrough pain with ABSTRAL
 - Limit consumption to treat four or fewer breakthrough pain episodes per day once a successful dose is found

FDA Product Approval Information for ACTIQ:

- FDA-approved indication:
ACTIQ is an opioid analgesic indicated only for the management of breakthrough cancer pain in patients 16 and older with malignancies who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain
- FDA-approved dosing information:
 - Initial dose of ACTIQ: 200 mcg
 - Individually titrate to a tolerable dose that provides adequate analgesia
 - No more than two doses can be taken per breakthrough pain episode
 - Wait at least 4 hours before treating another episode of breakthrough pain with ACTIQ
 - Limit consumption to four or fewer units per day once successful dose is found

FDA Product Approval Information for FENTORA:

- FDA-approved indication:
FENTORA is an opioid analgesic indicated only for the management of breakthrough pain in adult patients with cancer who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. Safety and efficacy of FENTORA in patients below the age of 18 years have not been established.
- FDA-approved dosing information:
 - Initial dose of FENTORA: 100 mcg



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- For patients switching from oral transmucosal fentanyl citrate to FENTORA, initiate starting dose of FENTORA in accordance with instructions found in full prescribing information
 - Initiate titration using multiples of 100 mcg FENTORA tablet
 - Individually titrate to a tolerable dose that provides adequate analgesia
 - No more than two doses can be taken per breakthrough pain episode
 - Wait at least 4 hours before treating another episode of breakthrough pain with FENTORA
 - Increase FENTORA dose when more than one dose per breakthrough pain episode is required for several consecutive episodes

FDA Product Approval Information for LAZANDA:

- FDA-approved indication:
LAZANDA is an opioid analgesic indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Breakthrough cancer pain defined as a transient flare of moderate-to-severe pain occurring in patients experiencing persistent cancer pain otherwise controlled with maintenance doses of opioid medication. LAZANDA must be used with around-the-clock opioid medication.
- FDA-approved dosing information:
 - Initial dose for all patients is 100 mcg
 - Individually titrate to an effective dose, from 100 mcg to 200 mcg to 400 mcg, and up to a maximum of 800 mcg, that provides adequate analgesia with tolerable side effects
 - Dose is a single spray into one nostril or a single spray into each nostril (2 sprays)
 - Maximum dose is a single spray into one nostril or single spray into each nostril per episode; no more than four doses per 24 hours
 - Wait at least 2 hours before treating another episode of breakthrough pain with LAZANDA

FDA Product Approval Information for ONSOLIS:

- FDA-approved indication:
ONSOLIS is an opioid analgesic indicated only for the management of breakthrough pain in patients with cancer, 18 years of age and older, who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Breakthrough cancer pain defined as a transient flare of moderate-to-severe pain occurring in patients experiencing persistent cancer pain otherwise controlled with maintenance doses of opioid medication. ONSOLIS must be used with around-the-clock opioid medication.
- FDA-approved dosing information:
 - Initial starting dose of 200 mcg ONSOLIS in all patients
 - Titrate using 200 mcg ONSOLIS film increments (up to a maximum of four 200 mcg films or a single 1200 mcg film) to adequate analgesia without undue side effects
 - Maximum is one dose per episode; no more than four doses per day; separate by at least 2 hours



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FDA Product Approval Information for SUBSYS:

- FDA-approved indication:
SUBSYS is indicated for the management of breakthrough pain in adult cancer patients, 18 years of age or older, who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

- FDA-approved dosing information:
 - Initial dose of SUBSYS: 100 mcg
 - Titrate to a tolerable dose that provides adequate analgesia using a single dose per breakthrough pain episode
 - Maximum is no more than 2 doses per breakthrough pain episode; limit consumption to 4 or fewer doses per day; wait at least 4 hours before treating another episode of breakthrough pain



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FENTANYL: ORAL, SUBLINGUAL, AND NASAL FORMULATIONS (cont.)

Resources: (cont.)

FDA Product Approval Information for Abstral, revised January 2011 by manufacturer

FDA Product Approval Information for Actiq, revised July 2011 by manufacturer

FDA Product Approval Information for Fentora, revised July 2011 by manufacturer

FDA Product Approval Information for Lazanda, revised June 2011 by manufacturer

FDA Product Approval Information for Onsolis, revised May 2010 by manufacturer

FDA Product Approval Information for Subsys, revised January 2012 by manufacturer